REMARKS

Claims 98-102 stand rejected under 35 U.S.C. §101 as allegedly not supported by either a specific and/or substantial asserted utility or a well established utility. Claims 98-102 also stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not supported by either a specific and/or substantial asserted utility or a well established utility so that one of ordinary skill in the art would allegedly not know how to use the claimed invention. Applicants respectfully traverse these rejections as discussed below.

Applicants have argued in previous communications that the teaching provided in the present application as filed, in view of subsequent confirmatory data, meets the utility requirement of 35 U.S.C. §101. Applicants explicitly incorporate by reference and reiterate all previously made arguments with respect to claim rejections under 35 U.S.C. §101 and under 35 U.S.C. §112, first paragraph.

In addition to the arguments presented in previous communications, Applicants submit that the teaching provided in the present application as filed, irrespective of any subsequent confirmatory data, meets the requirements of 35 U.S.C. §101 and the requirements of 35 U.S.C. §112, first paragraph, as discussed below.

The Rejections of Claims 98-102 under 35 U.S.C. §101

Claims 98-102 stand rejected under 35 U.S.C. §101 as allegedly not supported by either a specific and/or substantial asserted utility or a well established utility. Applicants respectfully traverse this rejection.

The Examiner states: "Therefore, because no known specific biological activity is described within the instant specification nor specifically associated with any nucleic acid that encodes the polypeptides of SEQ ID NO:17, because the specification merely discloses on page 55 that the human 'GFRα3 does not bind any of these [GDNF family member] molecules (Figure 9C)', and that 'GFRα3is thus an orphan receptor', the claimed polynucleotides have no specific nor substantial utility because further experimentation is also necessary at the time of filing the instant invention to attribute a

function and 'real world" utility to the claimed nucleic acid molecules" (page 6, first full paragraph).

Applicants respectfully disagree with the Examiner's characterization of the present invention. As discussed below, the specification provides multiple examples of the utility of the claimed nucleic acids, vectors, cells and processes. Thus, since the specification includes examples of use of the claimed invention, demonstrating specific and substantial utility, the "real world" utility of the claimed invention was demonstrated by the time of filing of the application. The discussion and examples of such use in the specification are also an asserted utility of the claimed invention.

Applicants also note that demonstration of any specific, substantial, and credible utility is sufficient to provide utility as required under 35 U.S.C. §101. See, for example, *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401, 1412 (Fed. Cir. 1992): "[t]o violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." and *E.I. du Pont De Nemours and Co. v. Berkley and Co.*, 620 F.2d 1247, 1260 n. 17, 205 USPQ 1, 10 n. 17 (8th Cir. 1980) "A small degree of utility is sufficient ... The claimed invention must only be capable of performing some beneficial function ... An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely ... In short, the defense of non-utility cannot be sustained without proof of total incapacity." (quoted in the M.P.E.P. (Eighth Edition), 2701.01, II, page 2100-33).

Moreover, the invention need not be better than other alternatives. As stated by the Federal Circuit "The patent statute does not require that a patentable invention be superior to all prior devices." (*Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 7 USPQ2d 1222 (Fed.Cir. 1988), cert. denied, 488 U.S. 956 (1988)). Similarly, the Federal Circuit stated that a finding that "an invention that is an 'improvement' is not a prerequisite to patentability" since it "is possible for an invention to be less effective than existing devices but nevertheless meet the statutory criteria for patentability." (*Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 1 USPQ2d 1196 (Fed. Cir. 1986)).

Examples of Uses of th Present Invention Demonstrated in the Specificati n

The specification demonstrates the use of the claimed molecules to activate cells and to provide assays. See, for example, the discussion at page 3, lines 12-15; page 4, lines 24-27 and 34-36; page 5, lines 4-6 and 12-15; page 6, lines 4-5; Example 10, and Figure 12, *e.g.,* page 56, lines 6-8 and 13-15. The following are some of the examples of uses of the claimed invention that are demonstrated in the specification.

Cell activation:

The specification describes assays using molecules including the novel GFRα3 molecules (nucleic acid and polypeptides).

As discussed at pages 55-56, the GFR family of receptors interact with Ret tyrosine kinase receptors to stimulate tyrosine phosphorylation, so that chimeric receptors (such as those of Example 10, page 56, lines 3-22) may be used to activate cells by tyrosine phosphorylation. The claimed polynucleotides have been used to produce chimeric GFRα3 receptors by combination with the transmembrane and intracellular domain of the Rse tyrosine kinase receptor to provide a construct useful for activation of cells in response to ligands, which may include antibody ligands (see, *e.g.,* page 10, page 56, lines 6-8 and Examples 10-12). Activation of cells may be desired for altering the physiological state of target cells, or for the production of desired cellular products that require cellular stimulation, or for marking or identifying cells as a result of the activation. Chimeric receptors have been used, for example, to activate target cells in studies of growth and proliferation of hematopoietic cells (Nakamura et al., J. Biol. Chem. **271**:19483-19488 (1996)).

Ligand Screening:

The specification discusses and demonstrates ligand screening methods using the claimed molecules (*e.g.,* GFRα3 nucleic acid and polypeptide molecules). Such ligands may be used as cell or tissue markers, as well as being used for their physiological actions. Moreover, identification of antagonists would provide means of reducing the tyrosine kinase activity associated with the GFRα3 receptor; it is well

known that tyrosine kinase activity is associated in many cells with cellular proliferation and cancerous growth.

Using chimeric GFRα3 receptors as described in Example 10 (page 56, lines 3-22) an assay for receptor dimerization induced by GFRα3 ligands was demonstrated. Applicants note that this assay was performed before the identification of the native ligand, demonstrating the use of the claimed invention **in the absence of knowledge of the natural ligand.** (See, *e.g.,* Example 10, pages 55-56 and Figures 10-12, Figure 12 showing data obtained using the chimeric GFRα3 receptor construct, and Example 12 showing an analogous assay with GFRα2.)

Using GFRα3 receptors or chimeric GFRα3 receptors as described in Example 10 one can assay for ligand-induced activity, including agonist activity of antibodies as described in Example 12, as well as for antagonist activity (page 56, lines 19-22). Note that this assay was also performed **in the absence of knowledge of the natural ligand.**

Such ligand-induced activity may be "kinase or phosphatase activity (*i.e.*, by autophosphorylation) of catalytic domain that is fused to the ligand-binding domain of an α-subunit receptor of interest" as disclosed on page 5, lines 12-15 of the present application.

Other uses

The specification thus demonstrates several uses for the claimed invention as indicated above. It will be understood that this listing of uses is not an exhaustive listing, but that it serves to demonstrate that, at the time of filing the application, substantial and credible uses of the invention, with real world utility, had been demonstrated and were disclosed in the application.

The specification thus provides multiple examples of the actual use of the subject matter of Claims 98-102, as discussed above, demonstrating that the claimed invention satisfies the utility requirement of 35 U.S.C. §101. Accordingly, Applicants respectfully submit that the rejections of Claims 98-102 under 35 U.S.C. §101 are overcome.

The Rejections of Claims 98-102 under 35 U.S.C. §112, First Paragraph

Claims 98-102 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not being supported by either a specific and/or substantial asserted utility or a well established utility so that one skilled in the art would not know how to use the claimed invention. Applicants respectfully traverse this rejection.

Applicants note that the specification includes multiple examples of the actual use of the subject matter of Claims 98-102, as discussed above. Thus, the specification provides several examples of specific and substantial utility for the present invention. The inventors, by their use of the invention, demonstrate that one skilled in the art would indeed know how to use the claimed invention. Accordingly, Applicants respectfully submit that the rejections of Claims 98-102 under 35 U.S.C. §112, first paragraph, are overcome.

CONCLUSION

Applicants respectfully submit that the rejections to Claims 98-102 are overcome by the above arguments. Accordingly, Applicants respectfully submit that Claims 98-102 stand in condition for allowance, and respectfully request the reconsideration and withdrawal of the rejections of Claims 98-102.

Please charge any additional fees, including the fees for extension of time, and any other fees due, or credit overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No. **39766-0065 A**.

Respectfully submitted,

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